UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,444	08/08/2001	Yi Li	PF116D1C1	9646

22195 7590 06/13/2003

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER
BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/13/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/923,444	Applicant(s) Li et al.
	Examiner Michael Brannock	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 3, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 14, 16-20, 22, 23, and 30-46* is/are pending in the application.

4a) Of the above, claim(s) *1, 14, 17-20, 22, and 23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *16 and 30-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Aug 8, 2001* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application: Claims and Amendments

1. Applicant is notified that the amendments put forth in the preliminary amendment, 10/16/01, and in Paper 6, 12/20/02, and in Paper 8, 4/3/03, have been entered in full.

2. Claims 1, 14, 16-20, 22-23, 30-46 are pending.

3. Claims 1, 14, 17-20, 22-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. The traversal is on the grounds that a search of Groups I-III would not be a serious burden on the examiner. This is not found persuasive for the following reasons:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) **or** distinct as claimed (see MPEP § 806.05- §806.05(I)): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the

invention obvious. In the instant case, although a search of the antibodies of Group III would overlap a search of the polynucleotides of Group I and the polypeptides of Group II, the searches would not be coextensive. In many instances, an antibody will have been known in the art before the protein antigen has been discovered - or the DNA that encodes the protein. Further, often the protein will be known by a name different than the name given the protein after the cloning of the nucleic acid - and may even be associated with a completely different activity than that ascribed to it when the nucleic acid was cloned. Thus, Groups I-III require divergent searches, and to search both inventions would be burdensome. Therefore, the restriction is maintained and made final.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The second application must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the second application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In the instant case, the preliminary amendment filed with the instant application amends page 4 to replace the term "NT74" of the parent application with "NTT4". This amendment

does not constitute a correction of an obvious clerical error. The artisan reading the 09/062815 application would have no idea that the recited "NT74" was meant to read "NTT4". Thus, this amendment introduces new matter into the specification relative to the 09/062815 application. Therefore, the instant application cannot be a divisional application of 09/062815, but is instead a continuation in part of 09/062815.

Drawings

5. The drawings are objected to because new Figure 1D indicates that it should be matched with Figure 1E. According to page 9 of the preliminary amendment new Figures 1A-D are to replace Figures 1A-1E. Thus, there does not appear to be a Figure 1E that could be matched to the new Figure 1D. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim requires an antibody against the polypeptide of claim 14. The phrase "antibody against the polypeptide" renders the claim indefinite because it is unclear what the phrase is intended to encompass, e.g. it is unclear if the antibody was to have been raised against the polypeptide or simply have some affinity to the polypeptide or some other property. Therefore the metes and bounds of the claim cannot be determined. It is suggested that the phrase "an antibody raised against the polypeptide of claim 14" would be definite.

Additionally claim 14 requires "analogs" and "derivatives" of the polypeptide, yet the specification and claims do not provide a method for establishing the extent of derivation allowed by the claims, therefore the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16 and 30-46 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The

claims are directed to antibodies binding polypeptides of SEQ ID NO: 2. The specification does not appear to assert a use for the antibodies other than in the identification of the polypeptide of SEQ ID NO: 2, e.g. pg 3. The instant specification puts forth that the polypeptide is a member of the neurotransmitter transporter family and is about 95% identical to a rat neurotransmitter, pg 4. Presumably, the specification is referring to the protein described by Liu et al., FEBS Lett. 315(2)114-118, 1993 and also to the protein described by Mestikawy, et al., J. Neurchem. 62(445-455)1994. Both Liu et al. and Mestikawy, et al. describe the protein as an atypical or unusual member of the transporter family whose biological properties remain a mystery, see the Introduction of Liu et al. and the Abstract of Mestikawy, et al. Similarly, the instant specification provides insufficient information such that claimed antibodies, or polynucleotides or polypeptides could be used in a way that constitutes a specific or otherwise substantial utility.

The instant specification puts forth that the polypeptide is useful in a screening method to determine what ligands may activate or inhibit the polypeptide and also to determine what the physiological effects of the polypeptide might be (see page 18 example). This proposed use lacks a specific and substantial utility. It is not a specific use because any integral membrane protein could be used in exactly the same way. Further, many polypeptides are known in the art, yet the polypeptides have no known function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polypeptide.

Furthermore, the proposed use of the polypeptide to screen for ligands of the polypeptide or for biologic effects of the polypeptide is not a substantial utility. A substantial utility is a

practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of treating an unspecified disease or condition with a material that has no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the polypeptide could be involved in any number of disparate disease states, and could therefore be used as a diagnostic or therapeutic agent (see pages 3, 15, 17 and 20, for example). A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

The specification puts forth that the polynucleotides and polypeptides could be used as tissue specific or chromosomal markers, e.g. pages 19 and 20. Consistent with current examination guidelines, use as a tissue specific and/or chromosomal marker is not considered to be a substantial utility. Most every polypeptide exhibits some tissue specific pattern of expression and most every gene encoding a polypeptide is localized to some region of a

chromosome. However, without some assertion that the tissue or chromosomal localization can be used to practice a particular substantial utility, as in a marker for a particular disease state, the use of the polypeptides or polynucleotides as tissue or chromosomal marker does not constitute a substantial utility.

The specification puts forth that the polypeptide and/or polynucleotides could be used in forensic biology (page 20). However the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual. While one of skill in the art would appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to nothing more than an invitation to the skilled artisan to try and find such polypmorphisms if they exist.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

9. Claims 16 and 30-46 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Furthermore, claim 16 encompasses antibodies that bind an essentially limitless genus of polypeptide "analogs" and "derivatives" of the polypeptide of SEQ ID NO: 2, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 2; should Applicant establish a specific and substantial utility for the claimed antibodies, Applicant has not provided sufficient guidance as to how to make and use the antibodies to polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 2, but which still retain a desired property of the antibodies to the polypeptide of SEQ ID NO: 2. The specification has not provided guidance as to what properties of the antibodies to allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 2 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the antibodies to the protein corresponding to SEQ ID NO: 2 and those of variants of said protein. If an antibody to a variant of the protein corresponding to SEQ ID NO: 2 is to have a structure and function similar to the antibody to the protein corresponding to SEQ ID NO: 2, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 2, that will produce a useful antibody. Conversely, if an antibody to a protein variant of SEQ ID NO: 2 need not have a disclosed property, the specification has failed to teach how to use such an antibody.

The specification has failed to provide an activity or property of SEQ ID NO: 2 or of the antibodies to be used to evaluate the claimed variants for usefulness. The specification has not

provided a working example of the use of an antibody to a variant of the polypeptide of SEQ ID NO: 2 nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids of SEQ ID NO: 2 could be modified so as to produce a polypeptide that is not identical to SEQ ID NO: 2 and yet still retain the activity of the polypeptide of SEQ ID NO: 2.

While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. These or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 2 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing variants (e.g. pages 5), this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further

experimentation. Thus, due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and antigenic determination, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

10. Claims 16, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polypeptide of SEQ ID NO: 2, yet claim 16 encompasses antibodies that bind to polypeptides not described in the specification e.g. sequences from other species, mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would

not be able make useful predictions as to the amino acid positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polypeptide, that of SEQ ID NO: 2 with no instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 2, which is not sufficient to describe the essentially limitless genera encompassed by the claims. Additionally, claims 34 and 45 require human antibodies to the human protein SEQ ID NO: 2. There is no disclosure of such, and nor are such known in the art. Thus, the artisan would not expect that Applicant was in possession of human antibodies to SEQ ID NO: 2 at the time of filing.

Thus, with the exception of non-human or humanized antibodies that bind a polypeptide of SEQ ID NO: 2, the skilled artisan cannot envision encompassed variants. Therefore, only non-human and humanized antibodies that bind a polypeptide of SEQ ID NO: 2, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 16, 30-33, 36-39, 45 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Wadzinski et al., J. Biol. Chem. 267(24)16883-16888, 1992.

The claims require an antibody that binds a polypeptide that *comprises* the sequence of SEQ ID NO: 2. Thus, the polypeptides of the claims encompass proteins that have amino acid sequences *in addition* to that of SEQ ID NO: 2, e.g. carrier or tag sequences, and the claimed antibodies need only bind to those additional sequences and not to amino acids encompassed by SEQ ID NO: 2. The specification teaches that a protein comprising SEQ ID NO: 2 and an HA tag was expressed and isolated with an anti-HA antibody pg 25-26.

Wadzinski et al. disclose an anti-HA monoclonal antibody (12CA5) that binds the HA tag (see the Abstract). Further Wadzinski et al. teach that the antibody was commercially available (col 1 of pg 16884).

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

MB

June 12, 2003